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[Increased apoptosis and necrosis of coronary plaques in unstable angina]

[Article in German]

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In acute coronary syndromes, arteriosclerotic plaques are characterized by inflammation and decreased smooth muscle cell density. The underlying pathogenic processes remain unclear. Among others, increased programmed cell death (apoptosis) is postulated. Coronary atherectomy specimens from 26 patients with unstable angina (group 1) and from 24 patients with stable angina (group 2) were examined, using immunohistochemistry (TUNEL test to detect fragmented DNA) and transmission electron microscopy. The objectives of the present study were to evaluate plaque group differences in the cellular composition, to detect and quantify cell death, and to differentiate between apoptosis and necrosis. Group 1 lesions contained more macrophages and lymphocytes as well as significantly ($p = 0.01$) less smooth muscle cells compared with group 2 lesions, whereas both revealed a comparable cell density. All plaques showed signals for fragmented DNA. TUNEL-positive cells were seen more frequently in lesions with unstable angina ($p = 0.04$). Ultrastructural analysis revealed signs of programmed cell death, such as nuclear alterations, cellular condensation due to lost adhesion, and apoptotic bodies. Importantly, group I lesions comprised significantly more apoptotic SMCs and apoptotic macrophages compared with group 2 lesions (28% vs. 16%; $p = 0.02$). Also, cellular necroses were found to be increased in lesions with unstable angina (18% vs. 8%; $p = 0.02$). The density of macrophages showed a positive correlation to the incidence of cellular necroses in group 1 lesions ($r = 0.44$; $p = 0.02$), but not in group 2 lesions. In both plaque groups, this determinant was independent from cellular apoptosis, also at high levels as found with unstable angina. The present study on coronary atherectomy specimens with unstable angina reveals intimal macrophage infiltration and the density of apoptotic as well as necrotic intimal cells to be increased, whereas the content of intact SMCs was reduced. Increased, macrophage-independent apoptosis strongly points

to the presence of one or several pro-apoptotic intimal factor(s) predisposing to plaque rupture. Implications of our findings may be directed to identify this (these) factor(s) and to modulate endogenous apoptotic activity with the ultimate goal to raise regional smooth muscle cell density.

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